REMARKS

Applicant notes that some of the rejections made in this office action are newly applied while others are reiterated. Four areas of disagreement between Applicant and the Examiner are applicable to multiple pending claims. In the interests of simplifying the response to the rejections, these areas of disagreement will be discussed first, so that they may be referred to in brief in the sections below.

1. Chromosome maps

All pending claims require that chromosome maps be received as an input and that at least one data enhanced map, which includes gene- or protein-related data overlaid on a chromosome map, be displayed and provided as an output. The Examiner asserts that the definition of a chromosome map is "*A graphic representation of the positions of genes on chromosomes, obtained by observation of chromosomal bands or by determining the degree of linkage between genes*".

(A) Input of chromosome maps is not shown in Cuticchia.

In the current office action, the Examiner admits that Cuticchia does not teach the "direct inputting of chromosomal maps" but points to the paragraph bridging pages 469 and 470 of Cuticchia as suggesting that the "input data" described in the full paragraph on page 469 satisfies this limitation. The paragraph in question describes the database software used to hold data. The data input to that database corresponds to hybridization data for specific clones and probes. The Examiner maintains that this is equivalent to inputting a chromosome map because such data is pertinent to the physical mapping of a genome. Given sufficient hybridization data and additional information, the degree of linkage between genes can be determined. However, hybridization data is not equivalent to degree of linkage data, and even degree of linkage data is not equivalent to a graphical representation that could be taken to be a chromosome map. A stack of lumber can be used to build a house; however, the stack is not the house.

In addition, Cuticchia is directed to a system for creating "contig" maps of chromosomes.

If the maps already existed, there would be no need for Cuticchia to create the maps. Hence, Cuticchia does not teach imputing chromosome maps.

(B) **Display** of a chromosome map on which gene- or protein-related data have been overlaid is not shown in Cuticchia.

The Examiner points to Figure 1 of Cuticchia as "*a map of a chromosome that is enhanced with hybridization data*". The cited figure shows a graphical representation in the form of a typical microtiter dish and is used to indicate if data is available for a particular clone and probe. The user can enter data by selecting a spot and then entering the data in question. The display indicates the presence of data not the data itself. There is no graphical representation of the positions of genes on chromosomes or linkage values. In other words, no chromosome map is displayed by Cuticchia, let alone one enhanced with data as specified in the base claims.

2. An identifier specifying a genetic location for the data items on the chromosome maps is not taught in Cuticchia.

The Examiner looks at the "*differences in degrees of hybridizations between clones in the chromosomes*" as the recited identifiers. Differences in degrees of hybridizations between clones do **not specify a genetic location** absent additional information.

In addition, the Examiner points to the identifying code string "L67A12" as the recited identifier, as it "*specifies the location of the corresponding clone as row A, column 12 of plate 67 within sub-library of chromosomal data*". The recited code string indicates the location of hybridization data for that clone among a matrix of clone-containing wells within the display that is modeled as ***a titration plate*** and the location of where data related to that clone is stored ***within a database***. Neither location is equivalent to the location of data related to the location of **a gene on a chromosome map**, as defined by the Examiner.

3. Matching the location-specifying identifiers with predefined identifiers on a chromosome map is not taught in Cuticchia.

The Examiner interprets the hybridization measurements indicated graphically in Figure 1 as the predetermined identifiers, stating that these data are "*matched within a matrix wherein each cell corresponds to a different location in the library chromosome data (Figure 2B of Cuticchia et al.)*". First, the hybridization measurements are not predetermined, as they are experimentally determined data. Second, as noted above, storage locations within the chromosomal library database are not locations on chromosomal maps, as defined by the Examiner. The locations depend on the manner in which the database is structured. The Examiner has not pointed to any teaching in Cuticchia that the database is structured such that locations in the database are determined by their relation to any parameter regarding the map locations of genes on a chromosome.

4. Reordering the data items to an order matching the order of the predetermined identifiers.

First, the Examiner points to the section "Integration of Physical Maps" in the paragraph bridging columns 1-2 on page 473 of Cuticchia, identifying the merging of "physical and chromosomal maps ... based on their contents" as the recited reordering. The cited passage refers to comparing data from two different physical maps, "config" maps and "walking" maps of the same chromosome and resolving any inconsistencies in the maps. There is no teaching of any form of reordering of data items based any predetermined identifiers.

In addition, the Examiner points to the last paragraph of the introduction of Cuticchia as teaching "ordering the data according to properties in the data fields". The cited paragraph teaches the use of hybridization data to enable the ordering of clones into a "contig" map. There is no teaching regarding any "order" of the hybridization measurements, to which the contigs are matched.

The table below lists the pending claims ordered into three sets, showing the relevance of the above arguments to each set.

Claims	Relevant Arguments
Independent claim 1, dependent claims 2-3, 12-13, 15, 20-22, 24, 26-29, 55-56	**1(A & B), 2, 3, 4**
Independent claim 80, dependent claims 81-90, 92-94	**1(A & B), 2, 3, 4**
Independent claim 101, dependent claims 95-100	**1B, 2, 3**

The Examiner rejected Claims 1-3, 12-13, 15, 20-22, 24, 26-29, and 55-56 under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. [CABIOS, 1992, volume 8, pages 467-474]. Applicant traverses the rejection.

The Examiner states that Cuticchia teaches all the limitations of claim 1 except for the direct input of chromosome maps. The Examiner maintains that it would have been obvious to provide such an input, as "*giving chromosomal locations to genes in randomly organized libraries of genetic data gives a biological meaning to each gene in the mapping study from the initial steps of the process onwards [paragraph bridging pages 469-470 of Cuticchia et al. and Table I on page 468 of Cuticchia et al.]*."

First, in addition to the direct input of chromosome maps (limitation 1A noted above), claim 1 requires the limitations 1B, 2, 3 and 4 noted above. As discussed in detail above, Cuticchia does not provide these teachings.

Second, it is not clear how giving "*a biological meaning to each gene in the mapping study*", the motivation proposed by the Examiner for modifying claim 1 to input chromosome maps, would be of any benefit to the user of the CMAP interface of Cuticchia. Hence, Applicant submits that the Examiner has failed to make a *prima facie* case for obviousness with respect to claim 1 and the claims dependent therefrom.

Claims 3, 12, and 15 depend from claim 1 and include additional limitations. The grounds

the Examiner presents for rejection of claims 3, 12 and 15 with regard to the additional limitations all rest on the Examiner's interpretation of Figure 1 as showing a chromosome map. As noted above in section 1B, the graphic representation in Figure 1B is not a chromosome map. Hence, there are additional grounds for allowing claims 3, 12 and 15.

Moreover, the additional requirement of claim 15 is a relational database which stores a set of cross-referenced **tables for matching said identifiers (as they are read) with said predefined identifiers** through standard database queries. The Examiner points to the title and to Figure 1 of Cuticchia for this teaching, stating "*hybridization data are cross-referenced with the chromosomal contig data*". At most, Cuticchia teaches a database that matches names ("identifiers") like L67A12 with hybridization measurements, but as noted above in sections 2 and 3, those names and hybridization measurements are not the recited identifiers and predetermined identifiers. Hence, there are additional grounds for allowing Claim 15.

Claim 13 depends from claim 1 and additionally requires that the identifiers specifying a genetic location for each of said data items **be selected from published gene identifiers and symbols**. The Examiner states "*the data are selected from names of biomolecules published throughout the publication of Cuticchia et al*". Even if either of the Examiner's interpretations of the recited identifiers (discussed above in section 2) were accepted, the differences in degrees of hybridization not the code strings are "published" in Cuticchia prior to being "selected". Hence, there are additional grounds for allowing claim 13 and the claims dependent therefrom.

Claim 20 depends from claim 1 and further requires that co-location values be **statistically assessed** and that the **assessed co-location statistical significance be displayed** along side said gene- or protein-related data. The Examiner identifies the d(a,b) values of Cuticchia as the co-location values. Even with this definition, the Examiner has not pointed to any teaching of statistical assessment or display of d(a,b) values. In the current office action, the Examiner identifies the sum D of the d(a,b) values as the "*statistical quantity*" in question. Even if a simple sum could be taken as a statistical assessment, that sum is not a measure of **statistical significance** as the claim recites. The Examiner responds to Applicant's assertion that d(a,b)

values are not displayed as recited by stating "*these values of d(a,b) and D would be in effect displayed along side the location and identifier data as these data values are a data file accompanying the gene display*". A data file accompanying a "gene display" is not equivalent to a display of the data within that data file along side that "gene display". Hence, there are additional grounds for allowing claim 20.

Claims 21-22 and 55-56 depend from claim 1 and include additional limitations regarding the display of additional information characterizing the gene or protein related data along side the display of that data. The Examiner identifies the d(a,b) values discussed above as the additional information. As noted above with respect to claim 20, Applicant submits that these values are not displayed as recited. Hence, there are additional grounds for allowing claims 21-22 and 55-56.

Claim 22 depends from claim 21 and additionally requires that the additional information comprise annotations. The Examiner identifies the "hybridization data" of Figure 1 as the recited annotations. However, the Examiner has already interpreted the hybridization data (indicated in Figure 1 by the black, gray or white fills) as the recited data items received that are to be enhanced. Applicant submits that the "hybridization data" cannot be that data and also be the additional information characterizing that data. Hence, there are additional grounds for allowing claim 22 and the claims dependent therefrom.

Claim 26 depends from claim 21 and additionally requires that the data overlaid on the chromosome map be displayed as a scatter plot. The Examiner interprets Figure 1 as the recited scatter plot. If the Examiner's identification of Figure 1 as a chromosome map were accepted, the data displayed therein as a "scatter plot" is data that the Examiner interprets as specifying genetic locations and making up the recited chromosome map. These data cannot also be the data overlaid on the map. In the current office action, the Examiner states "*claim 26 does not limit which type of genetic or proteomic data (is) to be displayed*". Applicant respectfully disagrees. Claim 26 recites "**said** gene- or protein-related data" referring back to the base claim 1 recitation of gene- or protein-related data **overlaid** on chromosome maps. Accordingly, there are additional grounds for allowing Claim 26.

The Examiner rejected Claims 4-10 under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. as applied to claims 1-3, 12-13, 15, 20-22, 24, 26-29, and 55-56 above in further view of Koleszar et al. [US Patent 6,519,583; issued 11 February 2003; filed 27 July 1999]. Applicant traverses the rejection.

The Examiner states that Cuticchia teaches the limitations of claims 4-11, except for the limitations requiring particular display features. The Examiner looks to Koleszar for the missing teachings. The Examiner maintains that it would have been obvious to apply the display features taught by Koleszar to the method of Cuticchia to display "the genomic data in a more convenient and user-friendly format [see, for example, column 2, lines 5-9 of Koleszar et al.]".

As noted above with respect to claim 1, from which claims 4-11 depend, Cuticchia does not teach the base claim limitations discussed above in sections 1, 2, 3 and 4. Koleszar does not provide the missing teachings. In addition, the compression is applied to the overlaid gene- or protein-related data of Claim 1. As noted above in section 1B, Cuticchia does not provide a display of such data; hence, there is no display to apply the zooming operation identified by the Examiner as compressing the data in question. Accordingly, Applicant submits that the Examiner has not made a *prima facie* case for obviousness with respect to claims 4-11.

The grounds the Examiner presents for rejection of claims 5 and 7 with regard to the additional limitations rest on the Examiner's interpretation of Figure 1 as showing a chromosome map. As noted above in section 1B, the graphic representation in Figure 1 is not a chromosome map. Hence, there are additional grounds for allowing claims 5 and 7.

The Examiner rejected Claims 14, 16-19, 23, 25, 30-37, 40-43, 80-83, and 86-89 under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. as applied to claims 1-3, 12- 13, 15, 20-22, 24, 26-29, and 55-56 above in further view of Schena et al. [PNAS, 1996, volume 93, pages 10614-10619]. Applicant traverses the rejection.

The Examiner states that Cuticchia teaches all the limitations of base claim 1, from which claims 14, 16-19, 23, 25, 30-37, 40-43 depend, and most of the limitations of base claim 80, from which claims 82-83 and 86-89 depend, looking to Schena as teaching the additional limitations. The Examiner maintains that it would have been obvious to apply the teachings of Schena to those of Cuticchia "because both studies analogously pertain to viewing data regarding chromosomal properties in the form of matrices". I have now made this point below.

First, as noted above with respect to base claim 1, Cuticchia does not teach the limitations discussed above in sections 1, 2, 3, and 4. Schena does not provide the missing teachings. .

Second, the statement by the Examiner that "*both studies analogously pertain to viewing data regarding chromosomal properties in the form of matrices*" is equivalent to stating merely that the studies are in analogous fields of art. This does not provide any motivation to actually apply the teachings of one study to the other. Accordingly, Applicant submits that the Examiner has not made a *prima facie* case for obviousness with respect to claims 14, 16-19, 23, 25, 30-37, 40-43, 80-83, and 86-89.

Claim 14 depends from claim 1 through claim 13 and additionally requires that the published gene identifiers and symbols recited in claim 13 be selected from at least one of the recited list of numbers, IDs and names. In rejecting claim 13, from which claim 14 depends, the Examiner identifies the data strings such as "L67A12" as the recited gene identifiers. These strings are clearly not chosen from the symbols recited in Claim 14. In the current office action, the Examiner points to the bottom left column of Table I on page 468 of Cuticchia regarding Chromosome 1-8. Even if the term "Chromosome 1-8" could be taken to be a gene identifier, the Examiner has not pointed to any teaching that this term corresponds to any of the numbers, IDs and names recited. A chromosome identifier merely specifies the chromosome on which the gene occurs. There are tens of thousands of genes on a chromosome. The Examiner's argument is equivalent to stating that giving the state in which a city is located is equivalent to the city's name. Hence, there are additional grounds for allowing Claim 14.

Claim 16 depends from claim 1 and additionally requires that the gene- or protein-related data comprise an expression matrix having rows and columns, wherein each said row of said matrix contains data values for a particular gene or protein across a set of measured samples, and results of each said measured sample are provided by data in respective columns of said matrix. The Examiner points to the matrix displays of Schena as providing these teachings.

The only matrix identified in Cuticchia is the structure that the Examiner identifies as the chromosome map. The same structure could not be the map **and** the data matrix in question overlaid on that map. Hence, there are additional grounds for allowing claim 16 and the claims dependent therefrom.

With respect to Claim 17, the Examiner has already identified expression matrices as chromosome maps; hence, the Examiner cannot now identify such matrix as the claimed gene- or protein-related data that does not specify genetic location on a protein map. Hence, there are additional grounds for allowing Claim 17.

Claim 18 includes a similar requirement to that of claim 16, that each row of the matrix be associated with a particular gene, with data in the respective row being associated with said particular gene. In the current office action, the Examiner states "Since each row of the microarrays in Figure 1 of Schena et al. is from *Arabidopsis*, each row of Figure 1 of Schena et al. is ASSOCIATED with each gene in *Arabidopsis*." First, only parts of only the first ten rows of the array in Figure 1 are from *Arabidopsis*. Second, association with a plurality of genes is not equivalent to association with a particular gene as specified. Hence, the same additional grounds exist for allowing claim 18 and the claims dependent therefrom as discussed above with respect to claim 16.

Claim 23 depends from claim 21. As noted above, Cuticchia does not teach the claim 21 requirement of a display of **additional information** characterizing the gene- or protein-related data along side of said display of that data and positioned relative to the respective locations on the chromosome map of the respective genes characterized by that data. In the current office

action, the Examiner states that Table 1 on page 10616 of Schena "*annotates the microarray of Figure 1 with gene ontology information comprising the Blast identity and the Accession numbers of each of the genes related to Arabidopsis*".

First, Table 1 is not displayed alongside Figure 1. Second, nothing in Table 1 is positioned relative to locations on a chromosome map. Hence, there are additional grounds for allowing claim 23.

Claim 30 depends from claim 18 and additionally requires that row vectors of the values in the rows of the matrix be calculated; using an auxiliary process to obtain cluster data for said row vectors; and **displaying said cluster data along side said display** of said arbitrary gene- or protein-related data. The Examiner points to Figures 1 and 2 of Schena, interpreting the left panel of Figure 2 as showing cluster data obtained from the values in Figure 1. The display along side the left panel of Figure 2 is another display of "cluster data" from a second experiment, not the data from which the left panel data was calculated. No part of Figure 2 is displayed alongside any part of Figure 1. Hence, there are additional grounds for allowing claim 30 and the claims dependent therefrom.

Claims 32 and 33 depend from claim 30 and additionally require that cluster data be displayed in a single column or a multi-column matrix respectively, **adjacent** each matrix of gene- or protein-related data. The Examiner points to the "heat map with color coding, in a column adjacent to the matrices, or in multiple columns next to the matrices" as providing these teachings, stating that the superposition of the colors is "*an obvious variant*" of displaying the same information adjacent the matrix. Applicant submits that the color coding in question constitutes the entire display of said arbitrary gene- or protein-related data identified by the Examiner. The claim requirement that the cluster data be positioned adjacent the arbitrary gene- or protein-related data allows both sets of data to be viewed simultaneously. Hence, the replacement of one set of data by the other set as suggested by the Examiner is not "***an obvious variant***", and there are additional grounds for allowing claims 32 and 33.

Claim 34 depends from claim 1 and additionally requires that the gene- or protein-related data comprises a matrix of at least one microarray of gene expression data, wherein (1) **each row of the matrix is associated with a particular gene**, and wherein (2) each column of the matrix is associated with a microarray experiment, wherein (3) a portion of the total number of columns is associated with experiments taken from **normal, healthy tissue**, and another portion of the total number of columns is associated with experiments taken from **tissue exhibiting an abnormality**, said method further comprising (4) dividing the matrix into two smaller matrices with a first matrix containing the columns associated with normal experiments and a second matrix containing the columns associated with abnormal experiments, and wherein said matching and displaying are performed with regard to both first and second matrices

With respect to limitation (1), as noted above with respect to claim 16, Schena does not teach that each row of any of the matrices is associated with a particular gene.

With respect to limitation (3), the Examiner states that the columns in Figure 1A relate to normal tissue, as no heat shock is applied, while the columns in Figure 1B relate to "abnormal" tissue as heat shock is applied. Applicant submits that the claim uses the word "healthy" to qualify "normal" and specifies that the other category of interest is data from experiments taken from **tissue exhibiting an abnormality**. The distinction is not between tissues that are or are not subjected to abnormal conditions (heat shock) in the experiments, but between tissues that are intrinsically healthy or unhealthy before any experiments are carried out. Applicant maintains that these meanings of the terms normal and abnormal conform with the standard meanings typical in the art. Schena does not separate out columns of data in the matrices on the basis of this distinction as recited. Hence, there are additional grounds for allowing claim 34 and the claims dependent therefrom.

Claim 36 depends from claim 34 and additionally requires that a **relevance score** be calculated for at least one row of the matrices by comparing expression values in the first matrix with expression values in the second matrix, and **displaying** at least one calculated relevance score **along side** the row to which each pertains. The Examiner identifies the differential

expression profiles in Figure 2A of Schena as relevance scores. Even if the term "relevance score" were taken to encompass differential expression profiles rather than measures of *the separation value of the particular gene being analyzed*, as taught in the specification of the current invention (paragraph 0094), at most Schena displays expression values as the colors of matrix cells themselves, not along side any rows of cells, as the claim recites. In the current office action, the Examiner states that the color coding of cells is an "obvious variant" of a display alongside the cells. As noted above with respect to claims 32 and 33, Applicant submits that displaying data alongside cells allows that data to be viewed simultaneously with other data within the cells. Hence, the teachings of Schena are not an obvious variant of the claim requirement, and there are additional grounds for allowing claim 36 and the claims dependent therefrom.

Claim 41 depends from claim 36 and additionally requires that relevance scores be calculated and displayed in a binary code. The Examiner points to the binary codes in Table II in column 1 on page 472 of Cuticchia as providing this teaching. These codes are simply representations of the results of hybridization experiments and are not the results of any **calculation**. Hence, there are additional grounds for allowing claim 41.

Claim 42 depends from claim 36 and additionally requires that a plurality of relevance scores be calculated, said method further comprising **defining a relevance density score** based upon **distances between genetic locations and relevance scores**, and identifying **chromosomal locations** containing relevance density scores greater than or equal to the defined relevance density score. The Examiner points to Figure 1 of Cuticchia as providing these teachings, identifying the shadings of the circles as intervals of density scores. First, the shadings represent the presence of hybridization, the absence of hybridization, and the absence of a clone. Even if these could be interpreted as scores, no **densities** are involved. Second, the "hybridization distances d(a,b)" represent differences between profiles, not **distances** between genetic locations and relevance scores. Third, the locations indicated in the figure are not **chromosomal locations**. Hence, there are additional grounds for allowing these claims.

Claim 43 depends from claim 36 and additionally requires that the relevance scores be filtered by setting at least one relevance score limit value and displaying **only those relevance scores which are greater than or equal to at least one relevance score limit value**. The Examiner points to Figure 2 of Schena as providing this teaching, interpreting the color coding of data values in the cells of the matrix as filtering relevance scores between limit values. However, the claim also requires that data be excluded from display if the scores are less than one limit value. The only teaching of any data exclusion is in the figure legend, which teaches that some data values (each value being the average from two experiments) are not shown, based on the *relative spread* of results between those two experiments. This is not equivalent to teaching exclusion based on the average data value being less than any threshold value.

In the current office action, the Examiner states "the claims do not recite excluding the claim only recite filtering" arguing that thresholds for color differentiating between ranges of values is equivalent to the recited filtering. Applicant submits that exclusion or removal is intrinsic to the term filtering. See, for example the definitions at http://dictionary.reference.com/browse/filter or at http://www.yourdictionary.com/filter for the term "filter". Whether the usage relates to a mechanical device "any substance, as cloth, paper, porous porcelain, or a layer of charcoal or sand, through which liquid or gas is passed to remove suspended impurities or to recover solids", to electronics "a circuit or device that passes certain frequencies and blocks others" or to an optical element "a device or substance that partially or completely absorbs certain light rays" the widely accepted definitions include the idea that some portion of an input is blocked or removed by the action of filtering. Hence, there are additional grounds for allowing claim 43.

Applicant submits that claim 80 and the claims dependent therefrom should be allowed for the same reasons discussed above with respect to claim 34, that the same additional grounds exist for allowing claim 82 and the claims dependent therefrom as those discussed above with respect to claim 36, and that the same additional grounds exist for allowing claims 88 and 89 as those discussed above with respect to claims 42 and 43 respectively.

The Examiner rejected Claims 38 and 84 under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. in view of Schena et al. as applied to claims 1-3, 12-19, 20-37, 40-43, 55-56, 80-83, and 86-89 above, and further in view of McCully [US Patent 4,383,994 issued 17 May 1983; filed 19 January 1982]. Applicant traverses the rejection.

The Examiner states that the combination of Cuticchia and Schena teaches all the limitations of claims 38 and 84 except for requiring that the relevance score comprise a "p value" and the relevance score be displayed as a value calculated by (-log p value). The Examiner looks to McCully for the additional limitations. The Examiner maintains that it would have been obvious to apply the teachings of McCully to those of Cuticchia/Schena to provide "improved and more advanced statistical analysis".

First, as noted above with respect to claims 1 and 80, from which claims 38 and 84 respectively depend, the combination of Cuticchia/Schena fails to teach the limitations 1, 2, 3 and 4 discussed above. McCully does not provide the missing teachings.

Second, as noted above with respect to claims 36 and 82, from which claims 38 and 84 respectively also depend, the combination of Cuticchia/Schena fails to teach the requirement that a relevance score be calculated for at least one row of the matrices by comparing expression values in the first matrix with expression values in the second matrix, and **displaying at least one calculated relevance score along side the row to which each pertains**. McCully does not provide the missing teachings.

Accordingly, Applicant submits that the Examiner has not made a *prima facie* case for obviousness with respect to claims 38 and 84.

The Examiner rejected Claims 39 and 85 under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. in view of Schena et al. as applied to claims 1-3, 12-19, 20-37, 4043, 55-56, 80-83, and 86-89 above, and further in view of Ben-Dor et al. [Genome Research, 2000, volume 10, pages 365-378]. Applicant traverses the rejection.

The Examiner states that the combination of Cuticchia and Schena teaches all the limitations of claims 39 and 85 except for the calculation of a plurality of relevance scores and their display as a line map. The Examiner looks to Ben-Dor for the missing teachings. The Examiner maintains that it would have been obvious to apply the teachings of Ben-Dor to the method of Cuticchia/Schena as "*an alternate means of analyzing the mappings of chromosomes*".

First, as noted above with respect to claims 36 and 82, from which claims 39 and 85 respectively depend, the combination of Cuticchia/Schena fails to teach the limitations regarding limitations 1, 2, 3 and 4 discussed above. Ben-Dor does not provide the missing teachings.

Second, the Examiner has not suggested any benefit that would be gained by the method of Cuticchia/Schena in applying the "alternate means" of Ben-Dor. The number of possible alternate means of analyzing gene mappings is very large, and there is no obvious reason why the means of Ben-Dor would confer a particular advantage to Cuticchia/Schena absent the present application as a guide. In the current office action, the Examiner again states "*as line maps are an alternate means for mapping the same information using a substitute (are equivalents), it is adequate for an obviousness prior art rejection*". Applicant submits that to sustain an obviousness rejection in view of a combination of prior art references the Examiner must show that there is some **motivation** in the art that would cause someone of ordinary skill to combine the references, and that in making the combination, there was a reasonable expectation of success. A proper analysis in this situation requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure. *In re Vaeck*, 20 USPQ2d 1438, 1442(CAFC 1991). Applicant maintains that there is no suggestion in this case founded in prior art. Accordingly, Applicant submits that the Examiner has not made a *prima facie* case for obviousness with respect to claims 39 and 85.

The Examiner rejected Claims 44-47, 49, 52-54, 90, 92-93, 95, and 98-101 under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. in view of Schena et al. as applied to claims 1-3, 12-19, 20-37, 40-43, 55-56, 80-83, and 86-89 above, and further in view of Pollack et al. [Nature Genetics, volume 23, 1999, pages 41-46]. Applicant traverses the rejection.

The Examiner states that Cuticchia teaches all the limitations of claims 44-47, 49, 52-54, 90, 92-93, 95, and 98-101 except those relating to abnormal copy numbers, or the one-to-one correspondences between the third and fourth matrices and the first and second matrices, respectively. The Examiner looks to Schena as teaching the correspondences between matrices, but not that these additional matrices are related to chromosomal copy numbers. The Examiner looks to Pollack for the missing teachings. The Examiner maintains that it would have been obvious to "*to modify the chromosomal mapping techniques of Cuticchia et al. and Schena et al., by use of the color coded heat map plots of Pollack et al. wherein the motivation would have been that the use of such plots allow more conveniently acquired and well resolved data [see lines 13-17 of abstract on page 41 and Figure 5a of Pollack et al.]*" and to further "*modify differential gene expression to analyze abnormalities as in Cuticchia et al. and Schena et al. by use of the disease analysis by chromosomal copy number analysis as in Pollack et al. because it is obvious to substitute known elements in the prior art to yield a predictable result*".

As noted above with respect to claims 34 and 80, from which claims 44-47, 49, 52-54, 90 and 92-93 respectively depend, the combination of Cuticchia and Schena fails to teach limitations 1, 2, 3 and 4 discussed above, or the details regarding the row and column data, normal and abnormal tissue, and the matching and displaying being performed with regard to two matrices that are divided out from a single original matrix. Pollack does not provide the missing teachings. Accordingly, Applicant submits that the Examiner has not made a *prima facie* case for obviousness with respect to claims 44-47, 49, 52-54, 90 and 92-93 44, 46-47, 90 and 92-93.

Claim 45 additionally requires that the chromosomal copy number abnormality data be

displayed in third and fourth matrices, wherein each value in the third matrix is matched with the expression value in the first matrix having the same row and column location, and wherein each value in the fourth matrix is matched with the expression value in the second matrix having the same row and column location. The Examiner points to Figures 1 and 2 of Schena for this teaching, identifying the "matrices" in Figure 1 as first and second matrices and those in Figure 2 as the third and fourth matrices. However, the data in the "third" matrix relates to data from both "+Heat Shock" and "-Heat Shock" experiments, i.e. to both first and second matrices, and the data in the "fourth" matrix relates to data from another pair of experiments involving Phorbol Ester, that are not shown anywhere in matrix form, and are certainly not shown in the second matrix.

The Examiner points to "Microarray Preparation" [singular]) in column 2 on page 10614 of Schena as teaching "*the same microarray setup is used four times (no Heat shock, Heat Shock, no phorbol ester, phorbol ester). Thus, each of the four microarray setups corresponds to one of the four matrices wherein the location for each cell (i.e. row, column) within the microarray setup corresponds to the same gene expression analysis in each of the four matrices.*" At most, this suggests that the sample compositions within the cells at corresponding positions in four microarrays are the same. However, claim 45 requires that values in third and fourth matrices are matched not with corresponding samples but with corresponding expression values in first and second matrices respectively. The values in the fourth matrix (Figure 2B) are not matched with the expression values in the second matrix (Figure 1B). Accordingly, there are additional grounds for allowing claim 45.

Claims 46 and 92 also require that the chromosomal copy number abnormality data be provided in columns interlaced with the columns of expression data in the first and second matrices. The Examiner points to Cuticchia (paragraph bridging columns 1-2 on page 471) as providing this teaching. The cited passage teaches that data may be added to a database, to enter comments or other general information about clones, but it does not teach that data is provided in interlaced columns in matrices as required by the claim. The Examiner also points to Figure 5a of Pollack as teaching annotating matrices with chromosomal abnormality data. The cited figure

shows annotations superimposed on an image of an array, but does not show any column interlacing of data as recited. In the current office action, the Examiner states that interlacing is an obvious variant of annotating. Applicant submits that the recited column interlacing is a narrower and more specific requirement than merely superimposing data on an image as suggested by the Examiner. Absent any suggested benefit, Applicant submits there would be no motivation to expend the additional data processing resources to modify Schena to accomplish such interlacing. Accordingly, there are additional grounds for allowing claims 46 and 92.

Claims 53 and 54 depend from claim 45 through claim 49 and include additional limitations corresponding to those of claims 42 and 43 respectively, regarding relevance density scores and filtering. As noted above with respect to claims 42 and 43, the combination of Cuticchia/Schena does not teach the additional limitations. Pollack does not provide the missing teachings. Accordingly, there are additional grounds for allowing claims 53 and 54.

Claim 101 includes limitations 1B, 2 and 3 discussed above. As noted above with respect to claims 1 and 80, the combination of Cuticchia/Schena fails to teach these limitations. Pollack does not provide the missing teachings. Claim 101 additionally includes limitations corresponding to those of claim 45. As noted above with respect to claim 45, the cited prior art does not teach these additional limitations. Accordingly, Applicant submits that the Examiner has not made a *prima facie* case for obviousness with respect to claim 101 and the claims dependent therefrom.

Claims 95 and 98-100 depend from claim 101 and include additional limitations corresponding to those of claims 36, 39, 42 and 43. As noted above with respect to claims 36, 39, 42, and 43, the combination of Cuticchia/Schena does not teach the additional teachings. Pollack does not provide the missing teachings. Accordingly, there are additional grounds for allowing claims 95 and 98-100.

The Examiner rejected claims 50 and 96 under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. in view of Schena et al. in view of Pollack et al. as

applied to claims 1-3, 12-37, 40-47, 49, 52-56, 80-83, 86-89, 92-93, 95, and 98-101 above, and further in view of McCully [US Patent 4,383,994 issued 17 May 1983; filed 19 January 1982]. Applicant traverses the rejection.

The Examiner states that the combination of Cuticchia, Schena and Pollack teaches all the limitations of claims 50 and 96 except for requiring that the relevance score comprise a "p value" and the relevance score be displayed as a value calculated by (-log p value). The Examiner looks to McCully for the additional limitations. The Examiner maintains that it would have been obvious to apply the teachings of McCully to those of Cuticchia/Schena to provide "improved and more advanced statistical analysis".

First, as noted above with respect to claims 1 and 101, from which claims 50 and 96 respectively depend, the combination of Cuticchia/Schena fails to teach several of the base claim limitations. In the case of claim 50, which also depends from claim 49, the combination of Cuticchia/Schena also fails to teach the limitations of that intervening claim 49. Neither Pollack nor McCully provide the missing teachings.

Second, the additional limitations of claims 50 and 96 correspond to those of claim 38. As discussed above with respect to claim 38, the combination of Cuticchia/Schena fails to teach the requirement regarding the display of at least one calculated relevance score along side the row to which each pertains. Neither Pollack nor McCully provide the missing teachings. Accordingly, Applicant submits that the Examiner has not made a *prima facie* case for obviousness with respect to claims 50 and 96.

The Examiner rejected claims 48, 51, 94, and 97 under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. in view of Schena et al. in view of Pollack et al. as applied to claims 1-3, 12-37, 40-47, 49, 52-56, 80-83, 86-89, 92-93, 95, and 98-101 above, and further in view of Ben-Dor et al. [Genome Research, 2000, volume 10, pages 365-378]. Applicant traverses the rejection.

The Examiner states that the combination of Cuticchia, Schena and Pollack teaches all the limitations of claims 48, 51, 94, and 97 except for the use of line maps. The Examiner maintains that it would have been obvious to apply these teachings as "an alternate means of analyzing the mappings of chromosomes". First, there are a large number of means for analyzing the mappings of chromosomes. Absent the present application as a guide, the Examiner has not pointed to any teachings in the art that would cause someone of ordinary skill to make the modification selected by the Examiner.

Second, As noted above with respect to claims 44 and 90, from which claims 48 and 94 respectively depend, and claim 34, from which claim 51 depends, the combination of Cuticchia/Schena fails to teach limitations 1, 2, 3 and 4, discussed above. Neither Pollack nor Ben-Dor provides the missing teachings. In addition, the Examiner has not pointed to any advantage in using this alternate means of analyzing the mappings over any of the other possible alternate means in the prior art, absent the present application as a guide. Accordingly, Applicant submits that the Examiner has not made a *prima facie* case for obviousness with respect to claims 48, 94 and 51.

As noted above with respect to claim 95, from which claim 97 depends, the limitations corresponding to those of claim 36 regarding relevance scores are not taught by the combination of Cuticchia, Schena and Pollack. Ben-Dor does not provide the missing teachings. Accordingly, Applicant submits that the Examiner has not made a *prima facie* case for obviousness with respect to claim 97.

The Examiner rejected Claim 11 under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. in view of Koleszar et al. as applied to claims 1-10, 12-13, 15, 20-22, 24, 26-29, and 55-56 above in further view of Corcoran et al. [US PGPUB 2003/0224419; published; December 2003; filed 2 April 2003; benefit date 1 September 2000]. Applicant traverses the rejection.

The Examiner states that the combination of Cuticchia and Koleszar teaches all the

limitations of claim 11 except for displaying popup dialogs to display additional details relative to a selected portion of the display. The Examiner points to paragraph 132 of Corcoran for the missing teachings. The Examiner maintains that it would have been obvious to apply the teachings of Corcoran to those of Cuticchia/Koleszar as a known, alternate form of viewing relevant data.

As noted above with respect to claim 1, from which claim 11 depends, Cuticchia does not teach limitations 1, 2, 3 and 4 discussed above. Neither Koleszar nor Corcoran provide the missing teachings. Accordingly, Applicant submits that the Examiner has not made a *prima facie* case for obviousness with respect to claim 11.

Applicant submits that all claim amendments presented herein or previously are made solely in the interest of expediting allowance of the claims and should not be interpreted as acquiescence to any rejections or ground of unpatentability. Applicant reserves the right to file at least one continuing application to pursue any subject matter that is canceled or removed from prosecution due to the amendments.

Respectfully Submitted,

Calvin B. Ward
Registration No. 30,896
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Agilent Technologies, Inc.
Legal Department, M/S Dl429
Intellectual Property Administration
P.O. Box 7599
Loveland, CO 80537-0599
Telephone (925) 855-0413
Telefax (925) 401-1731